An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Robert Madsen on October .

1. Please rewrite the claims as follows:

1. A transgenic mouse whose genome comprises at least one transgene operatively linked to a promoter effective for expression of the transgene in the brain tissue of said mouse, the transgene/transgenes comprising a DNA sequence encoding a heterologous Amyloid Precursor Protein (APP) comprising at least the Arctic mutation (E693G) and an Alzheimer's disease (AD) pathogenic mutation or a mutation affecting AD pathogenesis, resulting in increased amounts of intracellular soluble Aβ aggregates, including Aβ peptides.

3. The transgenic mouse according to claim 1, wherein said promoter is brain tissue specific.

4. The transgenic mouse according to claim 1, wherein the endogenous APP is expressed or not expressed

6. The transgenic mouse according to claim 1, wherein said mutation affecting AD pathogenesis is a mutant apolipoprotein E, apolipoprotein J (clusterin), α1-antichymotrypsin (ACT) or biologically fragments thereof.

7. The transgenic mouse according to claim 1, wherein said AD pathogenic mutation is one of the APP mutations KM670/671DF, KM670/671DY, KM670/671EF or KM670/671EY.

8. The transgenic mouse according to claim 1, wherein said further AD pathogenic mutation is one of the APP mutations KM670/671NL, KM670/671NY, KM670/671NF, KM670/671KL, KM670/671DL or KM670/671EL.

9.The transgenic mouse according to claim 1, wherein the transgenic mouse expresses only one transgene which comprises only E693G and KM670/671NL, the Arctic mutation (E693C) and the Swedish mutation (KM670/671NL).

10. The transgenic mouse according to claim 1, additionally comprising integrated into the genome of the mouse a homologous targeting construct for at least one of the neprilysin or insulin-degrading enzyme (IDE) genes, whereby integration disrupts these genes through gene ablation (knock-out) and enhances Aβ-40 and/or Aβ-42 Arctic peptide production.

14. A method of producing the transgenic mouse according to claim 1, comprising

a) injecting into a mouse egg or embryo at least one transgene operatively linked to a promoter effective for expression of the transgene in the brain tissue of said mouse, the transgene/transgenes comprising a DNA sequence encoding a heterologous Amyloid Precursor Protein (APP) comprising at least the Arctic mutation (E693G) and an Alzheimer's disease (AD) pathogenic mutation or a mutation affecting AD pathogenesis; and

b) transferring said fertilized egg or said embryo microinjected with said at least one transgene to a female mouse so as to produce a transgenic mouse from said fertilized egg or said embryo.

15. The method according to claim 14, wherein said promoter is brain tissue specific.

16. The method of claim 14, method according to claim 14, wherein said endogenous APP is expressed or not expressed.

18. The method of claim 14, wherein said mutation affecting AD pathogenesis is a mutant apolipoprotein E, apolipoprotein J(clusterin), α1-antichymotrypsin (ACT) or biologically fragments thereof.

19. The method according to claim 14, wherein said AD pathogenic mutation is one of the APP mutations KM670/671DF, KM670/671DY, KM670/671EF or KM670/671EY.

20. The method according to claim 14, wherein said AD pathogenic mutation is one of the APP mutations KM670/671NL, KM670/671NY, KM670/671NF, KM670/671KL, KM670/671DL or KM670/671EL.

21. The method according to claim 14, additionally comprising integrated into the genome of the mouse a homologous targeting construct for at least one of the neprilysin or insulin-degrading enzyme (IDE) genes, whereby integration disrupts these genes through gene ablation (knock-out) and enhances Aβ-40 and/or Aβ-42 peptide production.

22. A method of screening agents potentially useful for treating, preventing or inhibiting Alzheimer's disease, comprising:

a) administering an agent to a first transgenic mouse according to claim 1

b) observing the ability of the first transgenic mouse to form Aβ peptides; and

c) comparing the ability of the first transgenic mouse to form Aβ peptides to the ability of a second transgenic mouse according to claim 1 to form Aβ peptides, the agent not being administered to the second transgenic mouse;

wherein a decrease in Aβ formation in the first transgenic mouse indicates that the agent is potentially useful for treating, preventing or inhibiting Alzheimer's disease.

23. (currently amended) A method of screening for potential diagnostic agents for Alzheimer's disease, comprising:

a) administering an agent to a first transgenic mouse according to claim 1 an agent;

b) observing the ability of the first transgenic mouse to form Aβ peptides; and

c) comparing the ability of the first transgenic mouse to form Aβ peptides to the ability of a second transgenic mouse according to claim 1 to form Aβ peptides, the agent not being administered to the second transgenic mouse;

wherein a decrease in Aβ formation in the first transgenic mouse indicates that the agent is potentially a diagnostic agent for Alzheimer's disease.

24. The transgenic mouse according to claim 8, wherein said AD pathogenic mutation is KM670/671NL.

25..The method according to claim 20, wherein said AD pathogenic mutation is KM670/671NL.

2. Cancel claim 2.

3. Delete the present title and insert -- Transgenic Mouse Expressing Arctic Mutation

E693G-

4, The restriction requirement mailed December 15, 2008 is withdrawn. All claims at the time of allowance were reviewed and seen as not being an undue burden on the examiner for examination as a single invention. Thus, there is no prohibition to obviousness type double patenting in a continuing application based on a restriction./election requirement in this application..

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

November 9, 2009